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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,747	09/17/2008	Yong-Mahn Han	0002838USU/4105	2538

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EXAMINER	
CROUCH, DEBORAH	

ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/574,747	HAN ET AL.	
	Examiner	Art Unit	
	Deborah Crouch	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2010; October 19, 2010*

.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1 and 3-6* is/are allowed.

6)☒ Claim(s) *7-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 April 2008* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The office action mailed August 17, 2010 is vacated. A non-final office action is below. See attached Interview Summary, October 19, 2010.

Applicant's arguments filed June 30, 2010 have been fully considered but they are not persuasive. The amendment has been entered. Claims 1 and 3-13 are pending.

The rejection under 35 U.S.C. 112, first paragraph, because the specification, while being enabling made in the office action mailed March 30, 2010 has been withdrawn.

The rejection under 35 U.S.C. 112, second paragraph made in the office action mailed March 30, 2010 has been withdrawn.

The rejections under 35 U.S.C. 103(a) made in the office action mailed March 30, 2010 is withdrawn.

Claims 1-6 are allowable

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 7 remains rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for reasons set forth in the office action mailed March 30, 2010. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 7 require pBCKI I, pBCKI II, pBCKIDT I and pBCKIDT II, which are not

readily available to the public from a reproducible source at the time of filing. Thus, a deposit of the plasmids needs to be made to meet the requirements for enablement.

Applicant argues Example 1 discloses the production of vectors pBCKI I, pBCKI II, pBCKIDT I and pBCKIDT II and those of skill in the art can easily make the vectors. Applicant argues the specification discloses the restriction enzymes, primers and the vector backbone. These arguments are not persuasive.

While the specification provides a detailed account for producing vectors comprising the components of pBCKI I, pBCKI II, pBCKIDT I and pBCKIDT II, there is no enablement for obtaining the exact vectors labeled pBCKI I, pBCKI II, pBCKIDT I and pBCKIDT II. For example, the vectors produced by the skilled artisan could have a nucleotide different from pBCKI I, pBCKI II, pBCKIDT I and pBCKIDT II, and thus would not be considered to be these vectors. Thus, to ensure the availability of the specifically labeled vectors pBCKI I, pBCKI II, pBCKIDT I and pBCKIDT II, a deposit as set forth in the previous office action is required.

Claims 8 and 9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated bovine fibroblast cell produced by introducing the vector according to claim 1 or 5 into an isolated bovine fibroblast cell and permitting the insertion of the DNA construct of the vector into the endogenous beta-casein gene by homologous recombination and an isolated bovine embryo produced by introducing the nucleus of the bovine fibroblast cell according to claim 8 into an enucleated bovine oocyte to produce a bovine embryo, does not reasonably provide enablement for an isolated bovine somatic cell produced by introducing which is

beta casein gene targeted with-the vector according to claim 1 or 5 into an isolated bovine somatic cell and permitting the insertion of the DNA construct of the vector into the endogenous beta-casein gene by homologous recombination and an isolated bovine embryo produced by introducing the nucleus of which is nuclear transferred with the bovine somatic cell according to claim 8 into an enucleated bovine oocyte to produce a bovine embryo. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

At the time of filing, only ES cells and fibroblasts were known to undergo sufficient population doublings for selection of transformed cell types. The fundamental problem with gene targeting of cells for nuclear transfer is that most cells only divide a limited number of times in culture and gene targeting requires that the few cells that actually take up the targeting construct must be permitted to grow (divide) until there are sufficient cells (Pennisi and Vogel (2000), page 1723, col. 3, parag. 1, lines 5-16). Thus at the time of the instant invention the skilled artisan would have needed to engage in an undue amount of experimentation to make and use the claimed invention.

Claims 12 and 13 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of generating transgenic cattle and a method for obtaining a desired protein from the milk of a cattle by a method comprising transferring a bovine donor fibroblast nucleus into a bovine enucleated oocyte and transfer to a bovine female recipient, does not reasonably provide enablement for the claims as written which are and cross species nuclear transfer for reasons set forth in

the office action mailed March 30, 2010. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

At the time of filing, only ES cells and fibroblasts were known to undergo sufficient population doublings for selection of transformed cell types. At the time of filing cross species nuclear transfer was unpredictable in that the different species could not support fetal development to term of other species embryos. Thus at the time of the instant invention the skilled artisan would have needed to engage in an undue amount of experimentation to make and use the claimed invention. To overcome this rejection claim 12, step 5 has to be limited to a female bovine recipient.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 10 and 12, step (2) states "occurring," but this verb is not consistent with the method step. Applicant could state "permitting" or "allowing" alone or with "to occur."

Claims 10 and 12 are confusing be cause "selection" is by drug sensitivity or drug resistance, not by homologous recombination. A suggestion is to delete the phrase "by homologous recombination."

Claim12 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: activation of the embryo between steps 4 and 5.

Claim13 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: all related to obtaining a large scale of desired milk proteins. Claim 13 contains no step steps for producing a large scale amount of milk proteins.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 8 is rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Sheng et al. Chinese Journal, of Biotechnology, May 2004, Vol. 20(3), pp. 361-365.

Sheng teaches a goat fibroblast cells comprising an ATIII DNA sequence inserted into the goat β-casein gene (). The fibroblast taught Sheng and that of claim 8 cannot be distinguished as once the recombination occurs, the cells have the same genotype. Any differences would be obvious, not affecting the structure or function of the fibroblast cell. knockin expression vector. The Sheng anticipates or makes obvious the subject matter of claim 8.

Claims 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sheng et al. Chinese Journal, of Biotechnology, May 2004, Vol. 20(3), pp. 361-365 and PgPub20050177878 published August 11, 2005, efd September 30, 2003 (Melo).

Sheng teaches a goat fibroblast cells comprising an ATIII DNA sequence inserted into the goat β-casein gene (abs., lines 13-19). The fibroblast taught Sheng and that of claim 8 cannot be distinguished as once the recombination occurs, the cells have the same genotype. Sheng offers motivation in stating gene targeting is a powerful tool in the production of recombinant proteins in the mammary gland (abs, lines 1-4).

Melo teaches transgenic bovines produced by nuclear transfer using a bovine fibroblast as donor, where the fibroblast contained an exogenous DNA construct comprising a β-casein 5' promoter segment operably linked to a gene encoding human growth hormone (parag. [0080-0085]). Fibroblasts comprising the hGH construct were selected and the nucleus of the fibroblast transferred to an enucleated bovine oocyte activated (parag. [0088] and [0094]). The reconstructed embryo is cultured to produce a bovine embryo comprising the DNA fragment integrated into the genome of the embryo's cells (parag. [0094]). The embryo is transferred to a recipient bovine for term

development (parag. [0096]). Thus, at the time of the instant invention, it would have been obvious to the ordinary artisan to produce an bovine embryo comprising a DNA sequence encoding ATIII inserted into the bovine β-casein gene given the teaching of fibroblasts comprising the insertion in view of Melo teaching the production of bovine nuclear transfer embryos by transferring a bovine fibroblast nucleus into an enucleated bovine oocyte as taught by Melo.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch whose telephone number is (571)272-0727. The examiner can normally be reached on M-Fri, 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Deborah Crouch/
Primary Examiner, Art Unit 1632

October 22, 2010